IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Dated: October 23, 2006

DAVID TYVOLL, WINTHROP D. CHILDERS
and PAUL CRIVELLI

HP Docket No. 200314080-1

Serial No. : 10/762,688

Examiner Jonathan R. Miller

Filed : January 21, 2004

Group Art Unit 3653

For : SORTING PARTICLES IN PARALLEL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

AMENDED BRIEF OF APPELLANTS

This Amended Brief is presented in opposition to the Examiner's rejection of claims 1-13 and 51 in the final Office action dated April 6, 2006. Pursuant to the Notification of Non-Compliant Appeal Brief dated September 22, 2006, this Amended Brief includes a correct copy of the claims involved in the appeal (no allowed, cancelled, objected to, or withdrawn claims). The Amended Brief is intended to replace the Brief of Appellants filed September 6, 2006.

I. REAL PARTY IN INTEREST

The real party in interest is Hewlett-Packard Development Company, LP, a limited partnership established under the laws of the State of Texas and having a principal place of business at 20555 State Hwy 249, Houston, Texas 77070, U.S.A. (hereinafter "HPDC"). HPDC is a Texas limited partnership and is a wholly-owned

affiliate of Hewlett-Packard Company, a Delaware Corporation, headquartered in Palo Alto, CA. The general or managing partner of HPDC is HPQ Holdings, LLC.

II. RELATED APPEALS AND INTERFERENCES

There are no known related appeals or interferences.

III. STATUS OF CLAIMS

The present application was filed on January 21, 2004, with original claims 1-40. A first Office action imposing a restriction requirement was mailed June 15, 2005. Appellants elected claims 1-21 and withdrew claims 22-40 in their response (dated July 12, 2005). A second Office action, in which claims 1-21 were rejected, was mailed October 20, 2005. Appellants canceled claims 14, 17, and 22-40; added new claims 41-52; and amended claims 1, 6, 9, and 15 in their response (dated January 18, 2006). A third (final) Office action was mailed April 6, 2006. In the final Office action, the Examiner rejected claims 1-13 and 51, and imposed another restriction requirement, which resulted in withdrawal of claims 15-21, 41-50, and 52 from consideration. Appellants did not amend or cancel any of the pending claims in their response (dated June 6, 2006).

Pending claims 1-13 and 51 are the claims at issue in this appeal.

IV. STATUS OF AMENDMENTS

No amendments have been made subsequent to the final Office action dated April 6, 2006. (Appellants filed a response (dated June 6, 2006) to the final Office action. The June 6 response introduced no amendments to the pending claims.)

V. SUMMARY OF CLAIMED SUBJECT MATTER

The summary is set forth in exemplary embodiments. Discussion about elements and recitation of claimed subject matter can be found at least at the locations in the specification and drawings cited below.

The claims at issue in this appeal are directed to a device for sorting particles in parallel (e.g., see Figures 1 and 2). The device comprises an input reservoir 24 configured to hold a mixture 26 of first particles (e.g., "A" particles or particles 60) and one or more second particles (e.g., "B" particles or particles 62)(e.g., see page 2, line 23, to page 3, line 3; page 4, line 21, to page 5, line 2; page 5, lines 26-30). The device also comprises a transport mechanism 74 configured to move portions of the mixture in parallel from the input reservoir by dielectrophoresis (e.g., see page 6, line 19, to page 7, line 24). The device further comprises a plurality of sorter units 22 (or 50), in fluid communication with the input reservoir and configured to receive the portions of the mixture (e.g., see page 2, line 23, to page 3, line 25). Each sorter unit 22 (or 50) is configured to selectively move at least one second particle (e.g., "B" particles or particles 62), if received in one of the portions, from a path 68 followed by first particles received in the one portion so that the at least one second particle follows a different path 70 (Figure 2)(e.g., see page 5, lines 26-30; page 7, lines 1-9; page 8, lines 25-31).

Specific references to portions of the application are provided with the understanding that nonreferenced portions of the application also may be relevant. As such, it should be understood that the claims are not limited by the particular references made above, but rather are fully supported by the entirety of the disclosure.

VI. GROUNDS OF REJECTION

In the final Office action, claims 1-13 and 51 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 6,221,654 to Quake et al. ("Quake") in view of U.S. Patent No. 6,432,630 to Blankenstein ("Blankenstein").

VII. ARGUMENT

The Examiner has improperly rejected Appellants' claims 1-13 and 51 under 35 U.S.C. § 103(a) over Quake in combination with Blankenstein. When the claims are reviewed under the current standards for obviousness as set by the Federal Circuit Court of Appeals and the Board of Patent Appeals and Interferences, the impropriety of the rejections becomes clear.

A. STANDARD OF REVIEW

Obviousness is a question of law based on (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). "In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). "If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

The Manual of Patent Examining Procedure sets forth three basic criteria that must be met to establish a *prima facie* case of obviousness (MPEP § 2143):

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. (citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991))

Teachings in a reference indicating that a proposed combination should not be made must be considered when determining whether there is a motivation to make the proposed combination. *In re Young*, 927 F.2d 588, 18 USPQ2d 1089 (Fed. Cir. 1991). For example, the proposed modification cannot render the prior art unsatisfactory for its intended purpose. *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Moreover, the proposed modification cannot change the principle of operation of a reference. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

The law is "clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references." *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted).

B. *THE CITED REFERENCES: QUAKE AND BLANKENSTEIN*

Each of pending claims 1-13 and 51 were rejected as being obvious over a combination of Quake and Blankenstein. This subsection provides a brief overview of the subject matter disclosed by each of these references.

Quake relates to a method and device for sorting polynucleotides based on size. However, Quake also discloses use of the device to sort cells. Figure 1, which is shown here to facilitate review, illustrates an embodiment of a polynucleotide sorting device disclosed by Quake:

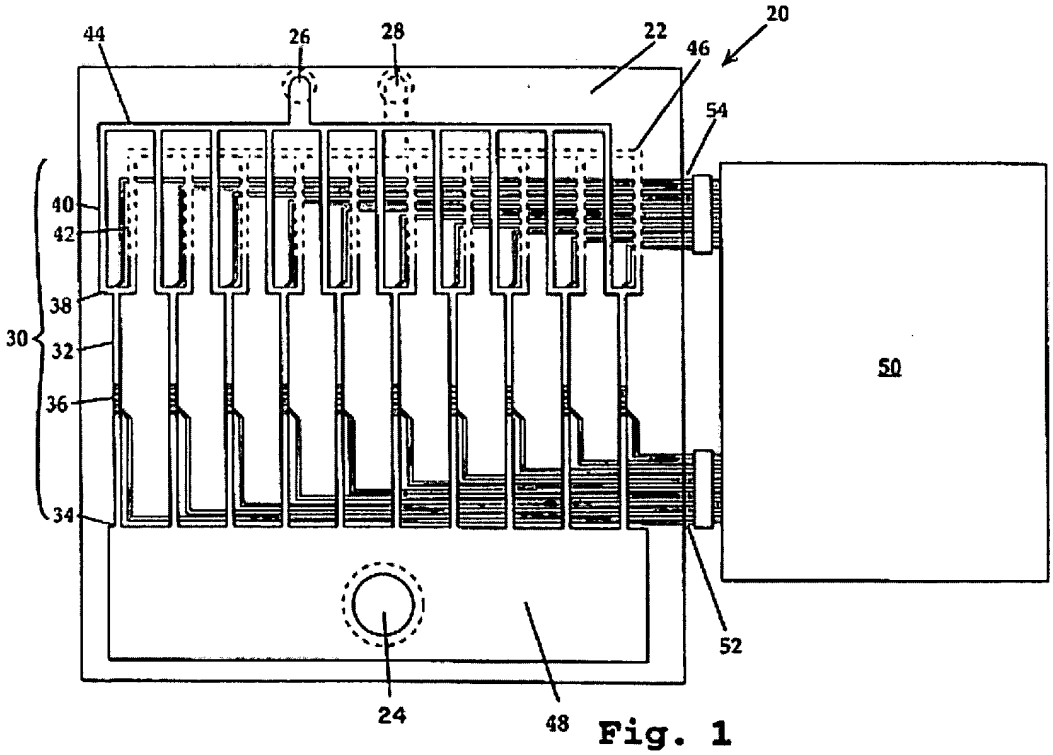


Fig. 1

Sorting device 20 has a solution inlet 24, two or more solution outlets, such as outlets 26 and 28, and a plurality of analysis units 30 arranged between the inlet and the outlets.

Each analysis unit is disclosed to be structured and to operate as follows. The analysis unit receives fluid and sample from a sample solution reservoir 48, which provides a fluid connection between solution inlet 24 and the analysis units. The analysis unit then selectively directs components (i.e., individual polynucleotides or cells) of the sample to outlet 26 or outlet 28. The analysis unit has a main channel 32 that receives sample from reservoir 48 via a sample inlet 34. Channel 32 also includes a detection region 36 for detecting sample components, and a discrimination region 38 disposed downstream of the detection region. Two or more branch channels, such as channels 40 and 42 extend in a branching fashion from the discrimination region. The discrimination region diverts individual sample components selectively to the branch channels based on a measured characteristic of each sample component, as detected by the detection region.

Quake discloses mechanisms for achieving bulk flow of fluid through the analysis units. In particular, polynucleotides/cells are introduced into the sample inlets (34) of Quake's sorting device by hydrostatic fluid flow created by a pump or pressure differential or by electroosmotic fluid flow created by electrodes (col. 3, lines 1-3; col. 14, lines 11-16).

Quake also discloses various sorting mechanisms to direct a particular molecule and/or cell into a selected branch channel from a discrimination region (col. 8, line 35, to col. 9, line 3). These sorting mechanisms include (1) electrophoretic discrimination (Figure 4A), (2) electroosmotic discrimination (Figure 4B), (3) a valve at the

discrimination region (Figure 4C), or (4) selective flow stoppage downstream of the destination region (Figure 4D).

Two of the sorting mechanisms of Quake involve electric fields. Figures 4A and 4B, which illustrate these two sorting mechanisms, are reproduced here to facilitate review:

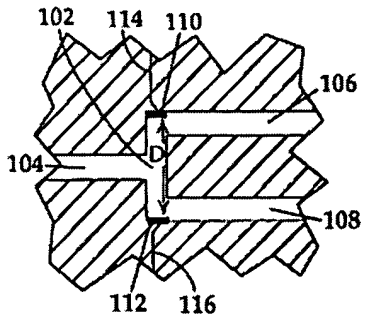


Fig. 4A

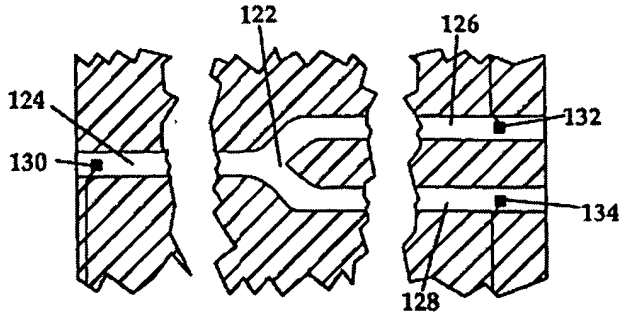


Fig. 4B

Figure 4A involves an electrophoretic (not dielectrophoretic) sorting mechanism. Electrodes 110 and 112 are disposed at a discrimination region 102 formed at the junction of main channel 104 and branch channels 106 and 108. More particularly, the electrodes are spaced transversely to create a transverse electric field that electrophoretically urges polynucleotides to either branched channel 106 or 108. Figure 4B involves an electroosmotic sorting mechanism. An electric field is applied to the ends of the channels via electrodes 130-134, to set up bulk solution flow (col. 14, lines 11-20).

Significantly, Quake discourages the use of electrophoretic and electroosmotic sorting mechanisms with cells. In particular, Quake states "since cells typically do not have predictable [ ] net charge, the directing means are preferably ones employing a valve in the discrimination region" (col. 15, lines 26-30).

Blankenstein relates to a micro-flow system for particle separation and analysis. Figure 1 illustrates the principle by which the system of Blankenstein separates particles:

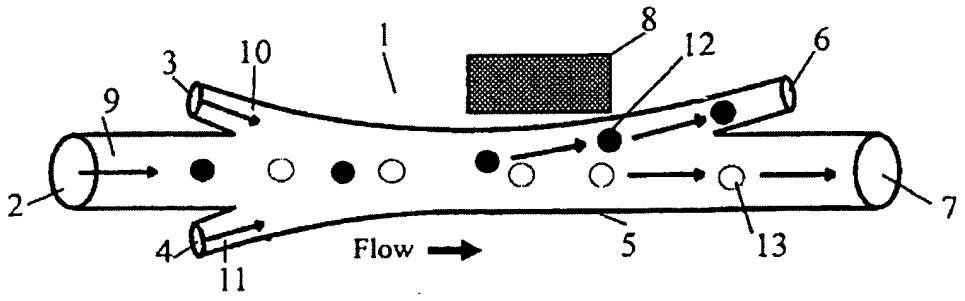


Fig. 1

Particles enter flow channel 5 by hydrostatic-driven fluid flow, guided by flow of guiding buffers 10 and 11, which enter flow channel 5 from ports 3 and 4. A separation mechanism such as a magnet 8 "generates a magnetic field across the flow channel 5," (col. 13, line 5; emphasis added by appellants'), to urge particles out of the main flow stream to sort outlet 6.

Blankenstein also discloses the use of dielectrophoresis for transverse particle separation, as illustrated in Figure 3:

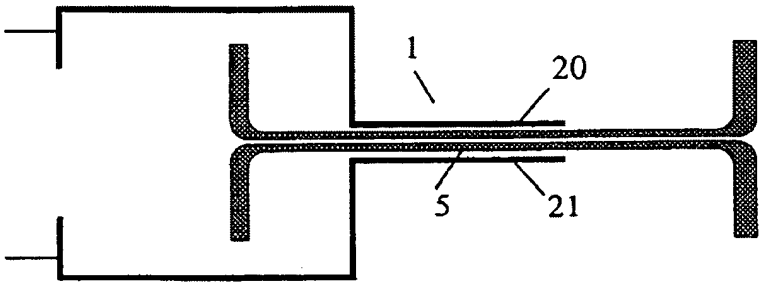


Fig. 3

Electrodes 20, 21 generate an electric field "substantially perpendicular to a longitudinal axis of the flow channel," (col. 14, lines 61-63). The electric field produces deflection of electrically charged particles "away from the sample containing particles flowing in the micro channel and into a guiding buffer," (col. 14, lines 65-67). Blankenstein thus discloses only a transverse separation role for dielectrophoresis, not a role in longitudinal transport.

Blankenstein also discloses an arrangement in which particle-separating forces are directed longitudinally rather than transversely. The arrangement is presented in Figure 11, which is reproduced here to facilitate review:

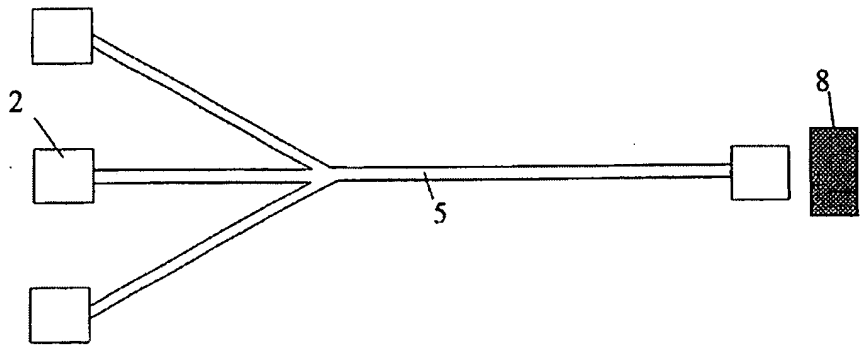


Fig. 11

A sample is introduced into separation channel 5 via inlet port 2. Particles in the sample are urged along channel 5 by a magnetic field generated by a magnet 8. However, Blankenstein does not teach or suggest a system with any type of electric field that urges particles longitudinally.

Blankenstein further discloses micro-flow systems with a serial array of assay sites disposed longitudinally. For example, Figure 12, which is reproduced here to

facilitate review, presents a system with an array of electrodes 59 arranged longitudinally along flow channel 5:

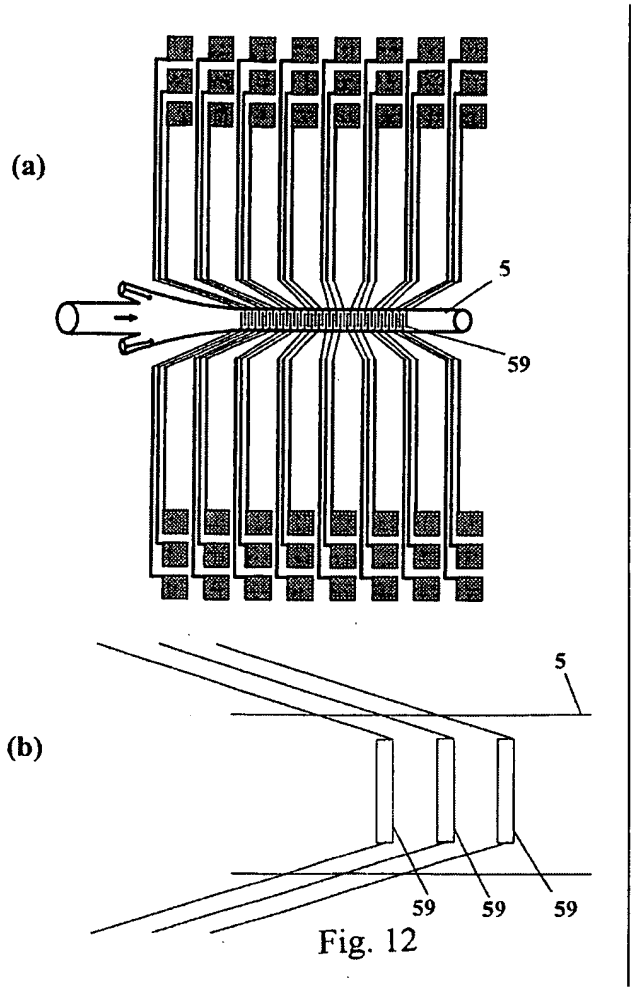


Fig. 12

However, the electrodes are <u>not</u> disclosed to be suitable for particle separation or for movement of particles along the channel. Instead, the electrodes are used to create an array of immobilized reagents. To create the array, a voltage is applied serially to the electrodes, to selectively immobilize probes, receptors, indicators, etc., at the electrodes when fluid with the probes, receptors, indicators, etc., is placed in the microfluidic channel 5 (see col. 18, line 63, to col. 19, line 20).

C. *THE CITED REFERENCES COMBINED DO NOT TEACH OR SUGGEST EVERY ELEMENT OF THE CLAIMS*

Independent claim 1 is directed to a device for sorting particles in parallel:

> 1. A device for sorting particles in parallel, comprising:
>
> an input reservoir configured to hold a mixture of first particles and one or more second particles;
>
> a transport mechanism configured to move portions of the mixture in parallel from the input reservoir; and
>
> a plurality of sorter units in fluid communication with the input reservoir and configured to receive the portions of the mixture, each sorter unit being configured to selectively move at least one second particle, if received in one of the portions, from a path followed by first particles received in the one portion so that the at least one second particle follows a different path,
>
> wherein the transport mechanism is configured to move particles by dielectrophoresis.

Neither Quake nor Blankenstein, taken alone or in combination, teaches or suggests every element of independent claim 1. For example, the cited references do not teach or suggest the transport mechanism recited by claim 1. In particular, the cited references do not teach or suggest a transport mechanism that moves particles by dielectrophoresis and that moves portions of a particle mixture in parallel from an input reservoir for receipt by a plurality of sorter units in fluid communication with the input reservoir.

Quake does not teach or suggest any use of dielectrophoresis, and particularly does not teach or suggest a transport mechanism that moves particles by dielectrophoresis, as explained above in subsection B of this section. In the final Office action, dated April 6, 2006, the Examiner reached the same conclusion: "Quake et al.

fails to disclose the transport mechanism is configured to move particles by dielectrophoresis" (page 4, lines 12 and 13). However, the Examiner states that "Quake et al. further discloses a transport mechanism [ ] configured to move particles by electrophoresis" (page 4, lines 11 and 12). Appellants disagree with the Examiner's characterization of Quake. Quake discloses an electrophoretic sorting mechanism (Figure 4A) for moving *polynucleotides* locally in relation to the discrimination region of an analysis unit. Quake does not teach or suggest an electrophoretic transport mechanism that moves portions of a mixture (and particularly not portions of a *particle* mixture) in parallel from an input reservoir for receipt by sorter units.

Blankenstein also does not teach or suggest a transport mechanism that moves particles by dielectrophoresis and that moves portions of a particle mixture in parallel from an input reservoir for receipt by sorter units. As described above in the preceding subsection, Blankenstein involves the use of dielectrophoresis for sorting particles, by generating a transverse electric field that moves particles laterally relative to the primary transport direction of the particles. The dielectrophoretic mechanism of Blankenstein has no apparent role in moving a portion of a particle mixture from an input reservoir for receipt by a sorter unit, as recited by claim 1. Instead, Blankenstein discloses fluid flow (e.g., Figure 1) as a transport mechanism for moving particles to a dielectrophoretic sorting mechanism.

However, in the final Office action, the Examiner stated: "Blankenstein discloses both electrophoretic and dielectrophoretic separation and the interchangeability of both techniques to achieve particle separation" (page 4, lines 17 and 18). Appellants note

that Blankenstein states: "Preferably, the electrodes are positioned in such a way that the electric field [for electrophoretic or dielectrophoretic separation] is essentially perpendicular to a longitudinal axis of the flow channel" (col. 6, lines 61-64). This arrangement of electrodes cannot provide particle transport from an input reservoir for receipt by a sorter unit and thus does not meet the characteristics of a transport mechanism recited by claim 1.

Quake and Blankenstein also particularly do not teach or suggest the additional limitation of claim 51. Claim 51 recites that "the dielectrophoresis includes traveling wave dielectrophoresis." In the final Office action, the Examiner asserted that "Blankenstein discloses the dielectrophoresis includes traveling wave dielectrophoresis" (page 6, lines 9 and 10). To support this assertion, the Examiner cited col. 18, lines 65+, of Blankenstein, which relates to Figure 12. Appellants strongly disagree. As described above in the preceding subsection, Figure 12 of Blankenstein relates to an array of electrodes for creating a corresponding immobilized array of probes, receptors, indicators, etc. The electrodes are not disclosed to be involved with dielectrophoresis of any kind, and particularly not traveling wave dielectrophoresis. Appellants thus maintain that Quake and Blankenstein, taken alone or in combination, do not teach or suggest traveling wave dielectrophoresis, as recited by claim 51.

Therefore, for at least these reasons, claims 1 and 51 should be allowed. Claims 2-13, which depend ultimately from claim 1, also should be allowed for at least the same reasons as claim 1.

D. *NO TEACHING, SUGGESTION, OR MOTIVATION TO COMBINE THE CITED REFERENCES*

It would not have been obvious to combine Quake and Blankenstein because there is no teaching, suggestion, or motivation to combine these references. Quake discourages the use of electric-field-based sorting mechanisms with cells. In particular, Quake states "since cells typically do not have predictable [ ] net charge, the directing means are preferably ones employing a valve in the discrimination region" (col. 15, lines 26-30). Accordingly, the teaching of Quake is at odds with the disclosure of Blankenstein. Quake thus directs one of skill in the art away from combining Quake and Blankenstein, by teaching that electric fields are not suitable for cell sorting.

Therefore, for at least these reasons, claim 1 should be allowed. Claims 2-13 and 51, which depend ultimately from claim 1, also should be allowed for at least the same reasons as claim 1.

E. *CONCLUSION*

For at least the reasons stated above, Appellants assert that there is no *prima facie* case of obviousness for rejection of the pending claims. In particular, the cited references, alone or in combination, do not teach or suggest every element of the claims. Furthermore, there is no teaching, suggestion, or motivation for combining the cited references. Accordingly, Appellants assert that the rejection of claims 1-13 and 51 under 35 U.S.C. § 103(a) as being obvious over Quake and Blankenstein is improper.

VIII. CLAIMS APPENDIX

1. (Previously Presented) A device for sorting particles in parallel, comprising:

an input reservoir configured to hold a mixture of first particles and one or more second particles;

a transport mechanism configured to move portions of the mixture in parallel from the input reservoir; and

a plurality of sorter units in fluid communication with the input reservoir and configured to receive the portions of the mixture, each sorter unit being configured to selectively move at least one second particle, if received in one of the portions, from a path followed by first particles received in the one portion so that the at least one second particle follows a different path,

wherein the transport mechanism is configured to move particles by dielectrophoresis.

2. (Original) The device of claim 1, further comprising a manifold configured to place the input reservoir in fluid communication with the sorter units.

3. (Original) The device of claim 2, wherein the manifold defines a conduit network that branches as it extends from the input reservoir to the sorter units.

4. (Original) The device of claim 1, wherein the transport mechanism is configured to provide continuous transport of the portions of the mixture, and wherein each sorter unit includes a pulse-activated transport mechanism configured to selectively move the at least one second particle.

5. (Original) The device of claim 1, wherein the mixture is disposed in a fluid, and wherein the transport mechanism is configured to apply at least one of a positive and a negative pressure to the fluid.

6. (Previously Presented) The device of claim 5, wherein the transport mechanism also is configured to apply a negative pressure to the fluid downstream of the plurality of sorter units.

7. (Original) The device of claim 1, further comprising one or more receiver structures in fluid communication with the plurality of sorter units and downstream thereof.

8. (Original) The device of claim 7, wherein the one or more receiver structures include a single receiver configured to receive first particles from each of the sorter units.

9. (Previously Presented) The device of claim 7, wherein the transport mechanism also is configured to apply a positive pressure to the fluid in the input reservoir.

10. (Original) The device of claim 7, wherein the one or receiver structures include a single receiver configured to receive the at least one second particle from at least two of the plurality of sorter units.

11. (Original) The device of claim 7, wherein each sorter unit is in fluid communication with a different receiver structure so that the at least one second particle moved by different sorter units are placed in different receiver structures.

12. (Original) The device of claim 11, wherein the different receiver structures are wells of a microplate.

13. (Original) The device of claim 1, wherein the mixture of first particles and one or more second particles is a mixture of different types of cells.

51. (Previously Presented) The device of claim 1, wherein the dielectrophoresis includes traveling wave dielectrophoresis.

IX. EVIDENCE APPENDIX

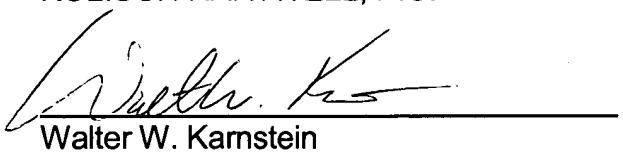
None.

X. RELATED PROCEEDINGS APPENDIX

None.

Respectfully submitted,

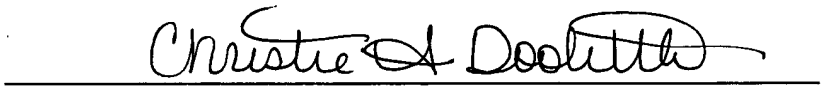
KOLISCH HARTWELL, P.C.



Walter W. Karnstein
Registration No. 35,565
520 S.W. Yamhill Street, Suite 200
Portland, Oregon 97204
Telephone: (503) 224-6655
Facsimile: (503) 295-6679
Attorney for Appellant

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on October 23, 2006.



Christie A. Doolittle